

### **REMARKS**

This submission is in response to the Official Action dated April 4, 2007. Claims 58, 60, 62-71, 89, 91-94, and 96 -125 are currently pending. Claim 125 is new and is supported by paragraph [0043]. Reconsideration of the above-identified application, in view of the following remarks, is respectfully requested. Each of the Examiner's rejections is discussed below.

#### **First Rejection under 35 U.S.C. §103**

Claims 58, 60, 62-64, 68-71, 89, 92, 93, 96, 98-103, 105-106, 108-114, and 117-124 have been rejected as obvious over WO 97/00076 to Morlet in view of Fox (U.S. Pat. 5,374,432) and further in view of Smith (U.S. Pat. 5,576,006). The Examiner states that Morlet teaches compositions containing biguanide polymer in topical treatments of microbial infection and further teaches the use of carriers. While the Examiner admits that Morlet teaches neither antimicrobial metallic materials nor moisture resistant films, she states that Morlet does teach compositions having further pharmaceutically active substances such as antimicrobials. The Examiner contends that Morlet can be combined with Fox which teaches a topical composition having an antimicrobial metal and an antibiotic. The Examiner also contends that Morlet can be combined with Smith, which teaches forming antimicrobial compositions, including biguanides, having a higher molecular weight that are more resistant to being washed away.

Applicants respectfully traverse. While the recent decision in *KSR International v. Teleflex Inc.*, 127 S.Ct. 1727, (2007) has altered the law on obviousness, the methods of the present invention are still non-obvious in view of the prior art. Obviousness is determined in accordance with the broader inquiry it previously set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966) which involved factual findings of: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) when relevant, objective evidence of non-obviousness. *Beckson Marine, Inc.*, 292 F.3d at 725-26. While the obviousness inquiry should look beyond the specific problem that the patentee was trying to solve, and includes, at the time of the invention "a known problem for which there was an obvious solution encompassed by the patent's claims," such is not the case for the presently claimed invention *KSR Int'l*, 127 S.Ct. at 1742. There is no reason a person of ordinary skill in the art would form the specific combination

of elements as recited in the present invention to be used in the method as claimed where the composition has (1) an organic polycationic polymer such as a biguanide polymer, (2) an antimicrobial metallic material (3) where the material is substantially water-insoluble or can be rendered substantially water-insoluble, (4a) a carrier selected from the group consisting of a cream, a lotion, a deodorant, a spray, a gel, a wax, an oil, an ointment, a soap, and an alcohol, and/or (4b) a skin-compatible component selected from the group consisting of emollients, thickeners, humectants, skin moisturizing agents, and surfactants, and/or (4c) a formulation which is a dermal antiseptic formulation, and/or (4d) a composition which can be administered by spreading or immersion and (5) wherein the composition forms a moisture-resistant film on the skin, which imparts (6) a persistent antimicrobial activity on the skin.

### ***Combining Morlet and Fox***

In particular, there is nothing in Morlet or Fox to suggest combining the Morlet polymer composition with a metallic material or combining the Fox metallic material with an organic polycationic polymer to form the moisture-resistant films used in the present invention. The reason provided by the Examiner is insufficient for combining these references. While both of these reference generically address adding “other compounds having antimicrobial activity such as bacitacin and trimethoprin” (Morlet, pg 10, lines 21-22) or combining “with a variety of antibiotics” which are “selected from among cephalosporin,  $\beta$ -lactam antibiotics, aminoglycoside antibiotics and quinoline antibiotics” (Fox, col. 1 lines 30 and 40 – 42), a person of ordinary skill in the art would not have been motivated “to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result” *Pharmaster Therapeutics, Inc., v. Viacell* 05-1490, -1551, pg. 37 (Fed. Cir., July 9, 2007) citing *in re O’Farrell*, 853 F.2d 894 903 (Fed. Cir. 1988). Neither Morlet nor Fox “gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.” *Id.*

The fact that other topical antimicrobials were known is insufficient to make the present invention obvious. The Examiner states that the combination of the metal and the polymeric antimicrobial material “flows logically from their having been individually taught in the prior art” and cites *In re Kerkhoven*, 626 F.2d 846 (CCPA 1980). However, the claims at issue in *In re Kerkhoven* required no more than the mixing together of two conventional spray-dried detergents to create a third spray-dried detergent. Such is not the case in the present invention which provides a moisture-resistant film that imparts a persistent antimicrobial activity. Further, there is no other reason prompted by the market or expectation of success which would motivate a

person of ordinary skill in the art at the time of the invention to combine these references. As stated by the Supreme Court, it is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *KSR Int’l*, 127 S.Ct. at 1727. The present invention does not randomly combine two antimicrobials but provides an organic polycationic polymer in combination with an antimicrobial metallic material since,

When a microorganism contacts the polymeric organic material of the present invention, the polymer engages or disrupts at least the outer portion of the lipid bilayer of the microorganism's cell membrane sufficiently to permit insinuation of the metallic biocide into the microorganism, where cell proteins or proteins in the lipid bilayer compete effectively for the biocide due to favorable binding constants... the metallic material preferentially binds to thiol and amine functional groups in proteins in the microorganism and thus is transferred directly from the matrix to the microorganism. The antimicrobial metal is subsequently transported intracellularly and causes cell death (para. [0020]).

Thus, without some specific guidance, reason, or motivation to combine Morlet and Fox, the general teachings of these reference combined with the knowledge of one of ordinary skill in the art is insufficient to make the present invention obvious. Therefore, even before examining the third reference (Smith) necessary to obtain each element of the claimed invention, the presently claimed invention is not obvious since the combination of an organic polycationic polymer with an antimicrobial metallic material for topical use is not obvious.

***Fox’s comment of Synergy***

The Examiner points to Fox’s statement that the silver salts exhibit synergistic effects with other antimicrobials as a motivation to combine each of Fox, Morlet, and Smith. However, this teaching in Fox is not as broad or effective as the Examiner suggests. Fox states that silver or a silver salt exhibits synergistic enhancement of efficacy when combined to form the compositions of the invention (col. 2, lines 29-32) and that the combination is with “a variety of antibiotics” (col. 2 line 30). When summarizing the scope of the antibiotics, Fox provides the closed list of antibiotics selected from cephalosporin, a  $\beta$ -lactam, an aminoglycoside antibiotic, or a quinoline antibiotic (see col. 1 lines 40-44). Exemplified antibiotics are the compounds: cephalosporin, tobramycin, norfloxacin,  $\beta$ -lactam and quinoline (see col. 1 lines 54-58) which are each non-polymeric compounds having amines, carboxylic acids, alcohol, ether, and amide

functional groups. These antibiotics are distinct from the polycationic antibiotics of the present invention. While the Fox background states to have found that a combination with "a variety of antibiotics" provide improved antimicrobial efficacy, this does not extend to all antibiotics. Fox provides support for his statement of synergistic behavior for a combination of a silver salt and tobramycin, pefloxacin, enoxacin, or aztreonam (see Fox, table V-A, col. 5). Pefloxacin, enoxacin, and aztreonam are piperazine-substituted naphthalene, piperazine-substituted naphthyridine, and an indole/thiazole compound, respectively. In contrast, the presently claimed invention is limited to polymers which are organic polycationic polymers, and which are preferably polymers having the biguanide moiety (i.e.,  $\text{NH}_2\text{-C}(\text{NH}_2)=\text{N-C}(\text{NH}_2)=\text{NH}$ ).

The teachings of Fox are insufficient to support a statement that all antimicrobials of any structure or mode of action have a synergistic effect when combined with silver. Thus, a person of ordinary skill in the art by his own knowledge or upon reading Fox would not consider that each and every antimicrobial combined with a silver salt would have a synergistic effect. Such a statement only supports a conclusion that the compounds tested by Fox and their structural counterparts have a synergistic activity. Read in any other way, a person of ordinary skill in the art as would consider the statement on synergy to be overreaching and an ineffective teaching. Thus, there is nothing in Fox to suggest combining the silver salt with any antimicrobial other than the piperazine-substituted naphthalene, piperazine-substituted naphthyridine, and indole/thiazole compound taught by Fox.

#### ***Combining Smith with Morlet and Fox***

The Examiner also contends that Morlet and Fox can be combined with Smith, which teaches forming antimicrobial compositions, including biguanides, having a higher molecular weight that are more resistant to being washed away. However, there is no reason provided either in Smith, Morlet, Fox, or available to one of ordinary skill in the art to combine the compositions for deodorizing footwear with both the antimicrobial compounds of Morlet and Fox. The Examiner contends that Morlet teaches that PHMB can be topically applied to the skin (Applicants disagree that Fox similarly teaches this, as stated by the Examiner on page 7 of the Action), Smith teaches the antimicrobial use of PHMB improved by forming a high molecular weight complex for deodorizing footwear, and that it would be obvious to provide the PHMB complex as provided by Morlet, the silver as provided by Fox, and the high molecular weight complex of Smith.

However, the rational underpinnings of this conclusion of obviousness are insufficient. *KSR Int'l at 1741* ("Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness" quoting from *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). Smith, as well as the understanding of one of ordinary skill in the art at the time of the invention, provides no motivation to combine the high molecular weight antimicrobial compounds with an antimicrobial metallic material. Smith teaches that an odor absorber, neutralizer, or perfume may be used in the complex (col. 3, lines 31 – 37). There is no suggestion to combine this complex with an antimicrobial material, particularly an antimicrobial metal material. Smith teaches that his composition is effective and has a lasting effect (see col. 3, line 21-25). Thus, he provides no motivation to combine the composition with an antimicrobial, much less the antimicrobial metallic material as presently claimed. In fact, this teaching is a disincentive to add further antimicrobials since it is already taught to be effective and long lasting. It is therefore counterintuitive to consider adding an antimicrobial agent such as a metallic material based on Smith or the knowledge of one of ordinary skill in the art.

Neither Morlet nor Fox form a film that is moisture resistant and has persistent antimicrobial activity. It would not have been obvious to one skilled in the art at the time this invention was made to combine the polymer and metallic material to form the moisture resistant film with residual antimicrobial action for extended periods after application of the composition.

It is not obvious to combine the teaching of one reference for a method of using a composition (Morlet, PHMB) with another reference teaching the use of the compound for a different purpose (Smith, PHMB) while simultaneously adding an agent from another composition (Fox, Ag). A person of ordinary skill in the art would not select such a combination as claimed in the present invention without some particular teaching or reasoning to do so.

Thus, claims 58, 60, 62-64, 68-71, 89, 92, 93, 96, 98-103, 105-106, 108-114, and 117-124 are not obvious over Morlet in view of Fox and/or Smith. Therefore, Applicants therefore request that this rejection be withdrawn.

**Second Rejection under 35 U.S.C. §103**

Claims 65-67, 91, 94, 97, 104, 107, and 115 – 116 are rejected as obvious over Morlet in view of Fox, Smith, and further in view of WO 95/17152 (the '152 publication). The Examiner contends that, while Morlet, Fox, and Smith do not teach forming an adduct with methylene-bis-N,N-diglycidylaniline, the '152 publication does, and it would be obvious to combine this compound, the silver iodide also taught in the '152 publication, and the composition taught by the combination of Morlet, Fox, and Smith. The Examiner additionally states WO '152 teach the antimicrobial compositions are safe for application to the body.

Applicants respectfully traverse. As discussed above, there is no motivation to combine Morlet with Fox and Smith. There is similarly no motivation to combine these references with an additional reference (WO '152) to arrive at the presently claimed invention.

The Examiner states that "Sawan et al. [WO'152] teaches that the adduct itself can be safely contacted with solutions meant for application to the human body to provide antimicrobial effects. Sawan et al. also teaches that silver iodide can be provided in such solutions to sterilize them." Applicants argue that such a statement, read out of context, can be misleading.

Just because WO'152 teaches both a dispenser and that solutions can be placed in the dispenser does not make any combination of the dispenser properties and the properties of any solution that may go into the dispenser obvious. WO'152 provides a dispenser having antimicrobial properties so that microbes within a solution in the dispenser (and therefore placed in contact with the coated walls of the dispenser) will be destroyed. Once the solution is removed from the dispenser (i.e., to be used as an eye rinse), no antimicrobials from the dispenser remain with the solution. This is an important aspect of the WO'152 publication since it provides a solution without microbial contaminants but without any antimicrobials in the solution. In solutions such as contact lens cleaning solutions, the ability to provide a solution without preservatives is important since many of the preservatives are toxic to mammalian cells as well as microbial cells (e.g., many preservatives used in the eye drop formulations are toxic to the goblet cells in the eye or the user develops chemical sensitivity to the preservative (see WO '157 pg. 2)). Therefore, if such a solution is applied to the human body, no antimicrobial effects from the silver and/or biguanide will be available.

While the adduct can be contacted with solutions and these solutions can later contact the human body, the solutions do not provide antimicrobial effects. The dispenser does. While a

Teflon-coated pan is used as a non-stick cooking surface, this used does not make it obvious to use Teflon in a lotion to keep skin from sticking. The substrates are completely different. Thus, it would similarly not be obvious to use the coating for the dispenser on skin.

Additionally, Sawan teaches the use of antimicrobial silver iodide, but Sawan does not teach putting silver iodide in such solutions to sterilize them. The adduct described in WO '152 is a non-leaching adduct. That means that it does not impart antimicrobial activity to a solution it comes in contact with. Without antimicrobial activity, the solution does not provide antimicrobial effects. In addition, the solution taught in WO'152 is a preservative-free sterile eye care liquid ('152 page 6 and 27). The fact that WO '152 exemplifies a liquid that may be used in the dispenser does not teach or suggest that that liquid is antibacterial, or that that liquid contains any of the dispenser coating components. WO '152 teaches how to substantially reduce the amount of dissolved silver (an antimicrobial) in the solution by passivating the silver-coated surface (pg 22 lines 23 – 25). Thus, WO'152 teaches away from adding antimicrobials to the solution.

The U.S. Supreme Court has indicated that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l*, 127 S.Ct. at 1727. For antimicrobials outside the scope as disclosed by Fox, there was no reason to prompt a person of ordinary skill in the art to modify the Sawan dispenser in such a way to form the topical composition as claimed in the presently claimed invention. In the absence of a reason to combine the teachings of the four different references, it was not obvious to do so.

Therefore, applicants respectfully request that the rejection under 35 U.S.C. §103 for claims 58, 60, 62-71, 89, 91-94, and 96-124 be withdrawn.

### **Double-Patenting**

All claims have been rejected by the Examiner under the judicially created doctrine of obviousness-type double-patenting as being allegedly unpatentable over various claims in commonly-owned U.S. Patents 6,180,584; 6,030,632; 5,869,072; and 5,817,325. Upon indication of allowable subject matter in the present application, the allowable subject matter not being patentably distinct from the claims of one or more of the above-cited patents, an appropriate terminal disclaimer will be timely filed.

\*

\*

\*

Therefore, in view of the above remarks, it is earnestly requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining that the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: September 4, 2007

Respectfully submitted,

By 

Lydia Gayle Olson

Registration No.: 48,487

DARBY & DARBY P.C.

P.O. Box 770

New York, New York 10008-0770

(206) 262-8900

(212) 527-7701 (Fax)

Attorneys/Agents For Applicant